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Synthesis and Transformations of Derivatives of 2-Aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carboxylic Acid

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Abstract—On the basis of methyl esters of 2-aryl-5-hydrazino-1,3-oxazole-4-carboxylic acids the earlier unknown methyl esters of 2-aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carboxylic acids as well as their functional derivatives were synthesized. The latter were used for further transformations, in particular, for introducing the residues of highly basic aliphatic amines into the 5 position of oxazole, and the oxazol-2-yl moiety into the 4 position of the oxazole ring.

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The functionalization of the 1,3-oxazole ring is one of the most important protocols for synthesis of new compounds promising for the search for various potential bioregulators.

Among the functionally substituted oxazoles the derivatives of 1,3-oxazole-4-carboxylic acid are of considerable interest. Various heterocyclic compounds were synthesized on their basis [1–3], and compounds possessing strong bactericidal and antiblastic activity were found [4–6]. Therefore, the development of new approaches to synthesis of substituted oxazoles with biophore substituents is a problem of today.

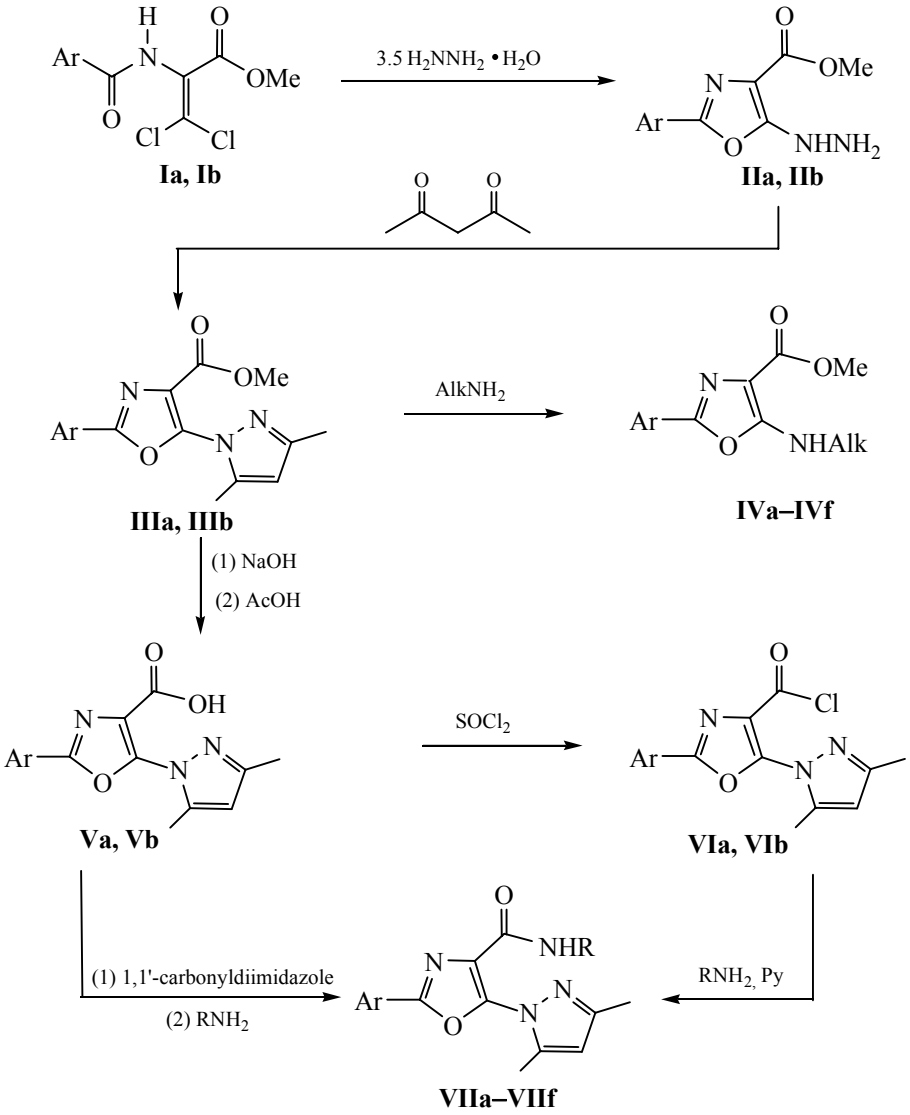
The goal of the present work was to synthesize the derivatives of oxazole-4-carboxylic acid having in the 4 position of the ring the 3,5-dimethyl-1*H*-pyrazol-1-yl moiety (Scheme 1), which is an important fragment in many biologically active organic compounds [7, 8].

The key products in all these transformations are methyl esters of 2-aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carboxylic acids **III** prepared by the sequence of transformations **I** → **II** → **III**. The first step in this process has been performed earlier [1], whereas the cyclization **II** → **III** is studied for the first time. Compounds **III** were used for the synthesis of acids **V**, that underlay the preparation of their acyl chlorides **VI** and N-substituted amides **VII** (Table 1) by the sequences of transformations **V** → **VI** → **VII** and **V** → **VII**. As follows from Scheme 1, the pyrazole ring remains intact in all processes. However, we have also studied the reactions of compounds **III** in which the pyrazole fragment plays the role of a good leaving group, which is typical f this structure [9, 10]. Thus, by heating compounds **III** with highly basic amines (monoethanolamine, its methyl ether, *N,N*-dimethylethylenediamine, benzylamine, furfurylamine) in dioxane the derivatives of 5-aminooxazole **IV** formed which cannot be prepared by the known oxazole cyclization [11, 12].

It should be noted that reaction **III** → **IV** can be complicated by the Cornforth rearrangement, which is typical for 4-carbonyl-substituted oxazoles [13–16]. Therefore, to unequivocally confirm the structure of the products of the reaction of the derivatives of 1,3-oxazole-4-carboxylic acid **III** with amines additional spectroscopic studies were required. To this end we have performed a complex ^{1}H and ^{13}C NMR study using the homonuclear COSY, NOESY and heteronuclear HMQC, HMBC experiments. All correlations are compiled in Table 2. Also, using the quantum-chemical program PRIRODA [17], the ^{13}C chemical shifts for structure **IVf** and a hypothetical structure of the Cornforth rearrangement **IVA** were calculated (see Fig. 1).

Comparison of the results of quantum-chemical calculations with the experimental data from Table 2

Scheme 1.



Ar = Ph (**I–VIa, VIIa, VIIc, VIIe**), 4-MeC_6H_4 (**I–IIIb, IVb–IVf, Vb, VIb, VIIb, VIId, VIIf**); Alk = CH_2CH_2OH (**IVa, IVb**), CH_2CH_2OMe (**IVc**), $CH_2CH_2NMe_2$ (**IVd**), CH_2Ph (**IVe**); CH_2–(furan-2-yl) (**IVf**); R = H (**VIIa, VIIb**), CH_2Ph (**VIIc, VIId**), 4-MeC_6H_4 (**VIIe, VIIf**).

suggests the formation of methyl esters of 4-oxazolecarboxylic acid **IV** rather than the alternative amides of the type **IVA**.

The full assignment of the signals in the ^1H and ^{13}C NMR spectra of compound **IVf** is given in Fig. 2.

The modification of substituents at the C^4 atom of the oxazole ring was performed by the example of amides **VIIa, VIIb** along the sequences of transformations **VII → VIII → IX**, as well as **IX → X → XII** and **IX → XI → XIII**. The final products of these transformations are the derivatives of 1,3-oxazole, which contain in the 4 position of the ring the 5-amino-4-cyano-1,3-oxazol-2-yl (compounds **XII**) or 5-amino-4-dimethoxyphosphoryl-1,3-oxazol-2-yl (compounds **XIII**) fragments.

The composition of all new oxazole derivatives shown in Schemes 1 and 2 was confirmed by elemental analysis (Table 1), and their structure, by the IR and ^1H NMR spectra (Table 3). Thus, the presence of the

Table 1. Yields, constants and elemental analysis data of compounds **III–XIII**

Comp. no.	Yield, %	mp, °C (solvent for crystallization)	Found, %			Formula	Calculated, %		
			C	H	N (Cl)		C	H	N (Cl)
IIIa	88	146–148 (EtOH)	64.73	5.15	13.99	$C_{16}H_{15}N_3O_3$	64.64	5.09	14.13
IIIb	92	143–145 (EtOH)	64.52	5.45	13.31	$C_{17}H_{17}N_3O_3$	65.58	5.50	13.50
IVa	45	144–147(EtOH)	59.47	5.30	10.77	$C_{13}H_{14}N_2O_4$	59.54	5.38	10.68
IVb	51	163–167 (2-propanol)	60.77	5.79	10.29	$C_{14}H_{16}N_2O_4$	60.86	5.84	10.14
IVc	58	108–111 (2-propanol)	62.12	6.19	9.71	$C_{15}H_{18}N_2O_4$	62.06	6.25	9.65
IVd	61	114–116 (MfCN)	63.25	6.95	13.87	$C_{16}H_{21}N_3O_3$	63.35	6.98	13.85
IVe	72	150–154 (EtOH)	70.89	5.75	8.64	$C_{19}H_{18}N_2O_3$	70.79	5.63	8.69
IVf	85	189–192 (EtOH)	65.31	5.21	9.02	$C_{17}H_{16}N_2O_4$	65.38	5.16	8.97
Va	95	210–212 (MfCN)	63.65	4.58	14.80	$C_{15}H_{13}N_3O_3$	63.60	4.63	14.83
Vb	93	192–195 (MfCN)	64.58	5.00	14.08	$C_{16}H_{15}N_3O_3$	64.64	5.09	14.13
VIa	89	142–148[a]	–	–	13.74 (12.28)	$C_{15}H_{12}ClN_3O_2$	59.71	4.01	13.93 (11.75)
VIb	91	126–132 [a]	–	–	13.47 (11.95)	$C_{16}H_{14}ClN_3O_2$	60.86	4.47	13.31 (11.23)
VIIa	88	189–192 (EtOH)	63.95	5.10	19.84	$C_{15}H_{14}N_4O_2$	63.82	5.00	19.85
VIIb	92	184–187 (EtOH)	64.98	5.51	18.61	$C_{16}H_{16}N_4O_2$	64.85	5.44	18.91
VIIc	85 (90)[b]	139–142 (2-propanol)	70.99	5.45	14.90	$C_{22}H_{20}N_4O_2$	70.95	5.41	15.04
VIId	79 (83)[b]	140–143 (2-propanol)	71.41	5.79	14.53	$C_{23}H_{22}N_4O_2$	71.48	5.74	14.50
VIIe	90	150–152 (EtOH)	70.90	5.45	15.00	$C_{22}H_{20}N_4O_2$	70.95	5.41	15.04
VIIf	86	190–194 (EtOH–DMF, 1:1)	71.43	5.69	14.31	$C_{23}H_{22}N_4O_2$	71.48	5.74	14.50
VIIIa	89	169–171 (MfCN)	47.46	3.48	13.01 (24.90)	$C_{17}H_{15}Cl_3N_4O_3$	47.52	3.52	13.04 (24.75)
VIIIb	92	164–168 (MfCN)	48.68	3.81	(24.14)	$C_{18}H_{17}Cl_3N_4O_3$	48.72	3.86	12.63 (23.97)
IXa	66	165–168[a]	–	–	12.48 (30.91)	$C_{17}H_{14}Cl_4N_4O_2$	45.56	3.15	12.50 (31.64)
IXb	60	170–174[a]	–	–	11.98 (29.91)	$C_{18}H_{16}Cl_4N_4O_2$	46.78	3.49	12.12 (30.68)
Xa	82	212–214 (MfCN–dioxane, 4:1)	53.62	3.15	17.61 (18.54)	$C_{18}H_{13}Cl_2N_5O_2$	53.75	3.26	17.41 (17.63)
Xb	79	213–215 (MfCN–dioxane, 4:1)	54.75	3.57	17.20 (17.47)	$C_{19}H_{15}Cl_2N_5O_2$	54.82	3.63	16.82 (17.03)
XI	86	130–134[a]	–	–	11.67 (19.78)	$C_{19}H_{20}Cl_3N_4O_5P$[c]	43.74	3.86	10.74 (20.39)
XIIa	86	261–263 (MfCN)	63.33	4.75	20.96	$C_{22}H_{20}N_6O_3$	63.45	4.84	20.18
XIIb	88	210–215 (MfCN)	67.29	5.61	19.52	$C_{24}H_{24}N_6O_2$	67.27	5.65	19.61
XIIIa	55	150–153 (toluene)	55.24	5.13	14.39	$C_{23}H_{26}N_5O_6P$[d]	55.31	5.25	14.02
XIIIb	62	158–162 (toluene)	57.86	5.60	14.18	$C_{24}H_{28}N_5O_5P$[e]	57.94	5.67	14.08

[a] Melting points are given for nonrecrystallized products. [b] Yields of compounds **VIIc, VIId** obtained by method *c* are given in brackets. [c] Found, %: P 5.81. Calculated, %: P 5.94. [d] Found, %: P 6.09. Calculated, %: P 6.20. [e] Found, %: P 6.15. Calculated, %: P 6.23.

pyrazole fragment is proved by ^{1}H NMR spectra, which contain the signals of two methyl groups at 2.20–2.21 ppm and the singlet signal C^4H at 6.11–6.19 ppm. The methoxycarbonyl group in compounds **III, IV** in the IR spectra is characterized by the absorption band in the range 1647–1721 cm^{-1}, and in the ^{1}H NMR spectra, by the singlet signals at 3.74–3.79 ppm. The participation of the dichlorovinylamide and trichloroethylamide fragments in cyclization of compounds **X** and **XI** can be concluded from the disappearance of the amide group signals in the IR spectra in the ranges 1640–1800 and 3000–3600 cm^{-1}. The presence of the cyano group in compounds **X** and **XII** is proved by the presence of strong bands at 2222–2229 cm^{-1} in the IR spectra. Finally, in the ^{1}H NMR spectra of all these compounds the signals of the aromatic and aliphatic protons with the proper ratio of integral intensities are registered.

Therefore, methyl esters of 2-aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carboxylic acids were

Table 2. NOESY, HMQC, HMBC correlations found for compound **IVf**[a]

^{1}H, δ, ppm	^{1}H, δ, ppm		^{13}C, δ, ppm	
	COSY	NOESY	HMQC	HMBC
2.32	7.27	7.27	21.66	130.33, 140.20
3.71	–	–	51.26	163.27
4.56	7.88	6.38, 7.88	40.58	160.08, 152.65, 108.27
6.38	7.58	4.56	108.27, 111.25	152.65, 143.23
7.27	2.32, 7.71	2.32, 7.71	130.33	21.66, 124.48, 130.33
7.58	6.38	–	143.23	108.27, 152.64
7.71	7.27	7.27	125.61	125.61, 140.20, 149.72
7.88	4.56	4.56	–	160.08

[a] For assignment of the signals in compound **IVf** see Fig. 2.

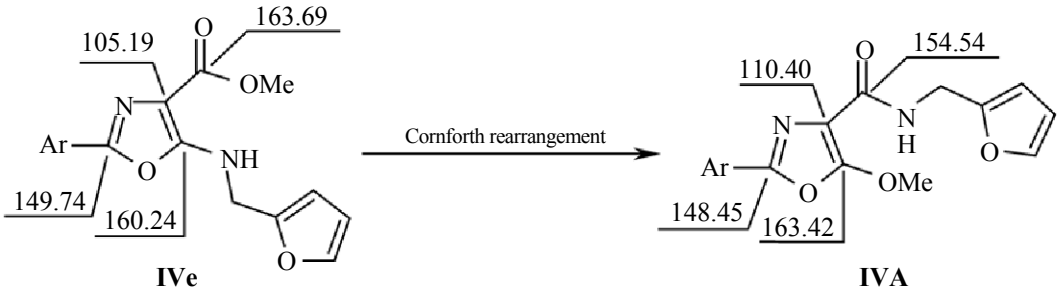


Fig. 1. Assignment of signals (ppm) in the ^{13}C NMR spectra of compound **IVf** and the hypothetical structure of the Cornforth rearrangement **IVA** based on quantum chemical calculations.

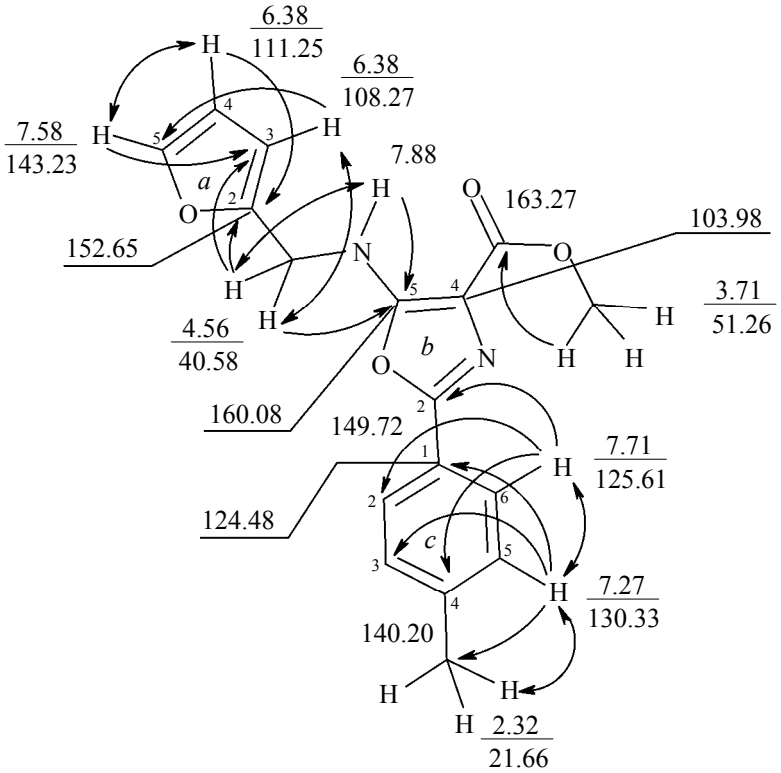
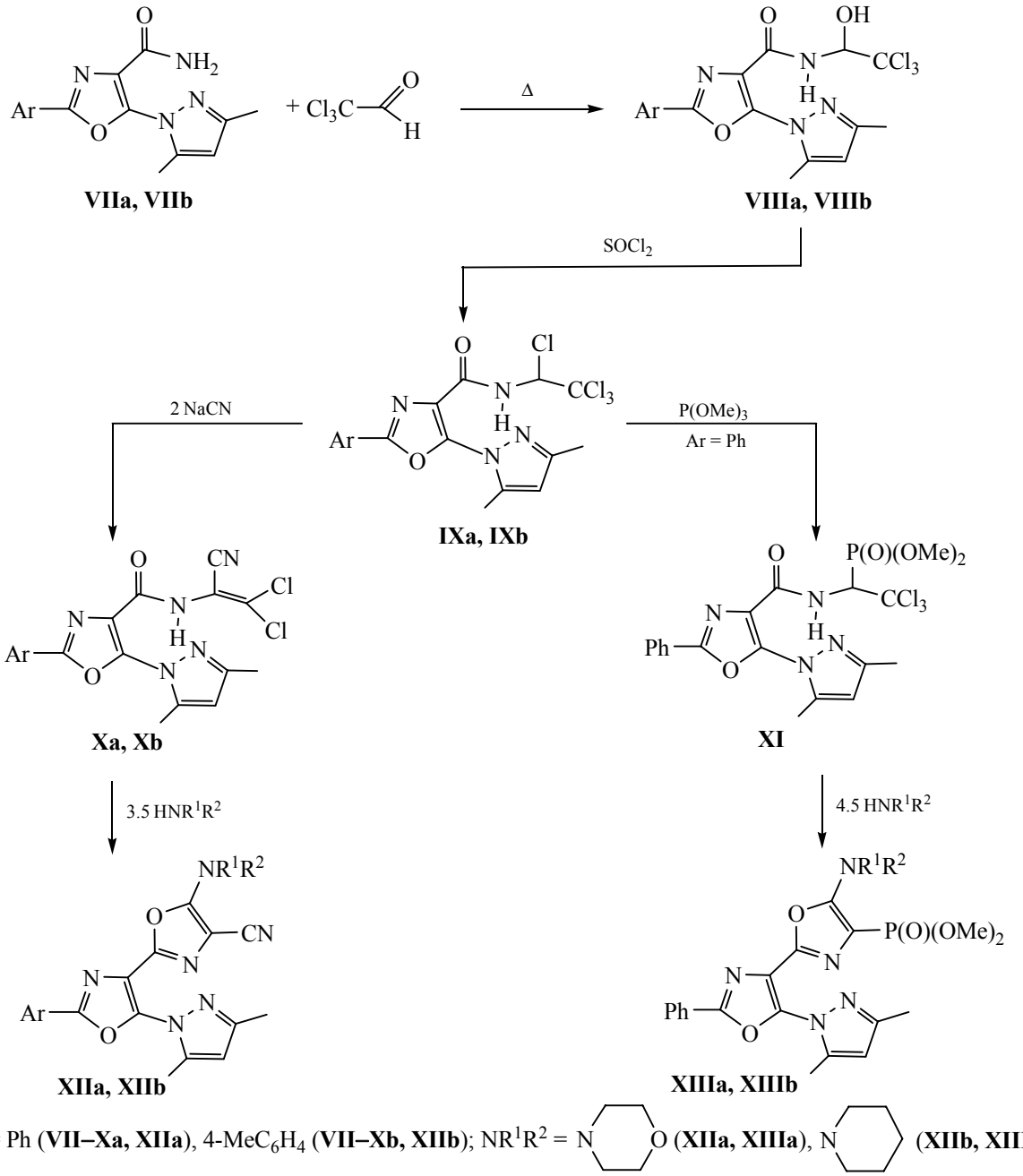


Fig. 2. Principal correlations (shown by arrows) and assignment of signals (ppm) in the ^{1}H and ^{13}C NMR spectra of compound **IVf**.

Scheme 2.



Ar = Ph (**VII–Xa, XIIa**), 4-MeC_6H_4 (**VII–Xb, XIIb**); NR^1R^2 = (**XIIa, XIIIa**), (**XIIb, XIIIb**).

synthesized and their reaction with highly basic aliphatic amines was studied; also, the modification of the 4 position of the oxazole ring was performed important for the search for compounds with various biological activity among the synthesized substances.

EXPERIMENTAL

IR spectra were taken on a Vertex 70 spectrometer in KBr, ^1H NMR spectra were recorded on a Varian VXR-300 spectrometer, ^1H–^{13}C NMR spectra with heteronuclear correlation were obtained on a Mercury-400 spectrometer (400 and 100 MHz, respectively) in DMSO-d_6, with TMS as an internal standard. Mass spectra were taken on an Agilent 1100/DAD/MSD VL G1965 instrument. Melting points were measured on a Fisher-Johns unit.

Methyl 2-acylamino-3,3-dichlorovinyl-acrylates (Ia, Ib) were obtained as described in [18].

Table 3. Spectral data for synthesized compounds **III–XIII**

Comp. no.	IR spectrum (KBr), ν, cm^{-1}	^1H NMR spectrum, δ, ppm (DMSO-d_6)
IIIa	1721 (C=O)	2.21 s (6H, $2CH_3$), 3.79 s (3H, OCH_3), 6.19 s (1H, CH), 7.61–8.02 m (5H, C_6H_5)
IIIb	1719 (C=O)	2.20 s (6H, $2CH_3$), 2.40 s (3H, CH_3), 3.78 s (3H, OCH_3), 6.19 s (1H, CH), 7.38–7.93 m (4H, C_6H_4)
IVa	1681 (C=O)[a], 3359 (NH, OH)	3.51–3.60 m (4H, $2CH_2$), 3.75 s (3H, OCH_3), 4.90 t (1H, OH), 7.32 m (1H, NH), 7.47–7.84 m (5H, C_6H_5)
IVb	1682 (C=O)[a], 3307, 3378 (NH, OH)	2.35 s (3H, CH_3), 3.49-3.59 m (4H, $2CH_2$), 3.74 s (3H, OCH_3), 4.89 m (1H, OH), 7.28–7.72 m (5H, C_6H_4, NH)
IVc	1673 (C=O)[a], 3365 (NH)	2.35 s (3H, CH_3), 3.29 s (3H, OCH_3), 3.56 m (4H, $2CH_2$), 3.74 s (3H, OCH_3), 7.31–7.72 m (5H, C_6H_4, NH)
IVd	1664 (C=O)[a], 3371 (NH)	2.21 s [6H, $N(CH_3)_2$], 2.35 s (3H, CH_3), 2.48–3.49 m (4H, $2CH_2$), 3.74 s (3H, OCH_3), 7.22 t (1H, NH), 7.29–7.74 m (4H, C_6H_4)
IVe	1647 (C=O)[a], 3366 (NH)	2.34 s (3H, CH_3), 3.75 s (3H, OCH_3), 4.60 m (2H, CH_2), 7.24–7.68 m (9H, C_6H_4, C_6H_5), 8.08 t (1H, NH)
IVf	1667 (C=O)[a], 3357 (NH)	2.32 s (3H, CH_3), 3.71 s (3H, OCH_3), 4.56 d (2H, CH_2), 6.38–7.71 m (7H, C_6H_4, C_4H_3O), 7.88 t (1H, NH)
Va	1708 (C=O), 2440 (OHass.)	2.21 s (6H, $2CH_3$), 6.17 s (1H, CH), 7.60–8.03 m (5H, C_6H_5), 13.61 br.s (1H, OH)
Vb	1731 (C=O), 2459 (OHass.)	2.22 s (6H, $2CH_3$), 2.41 s (3H, CH_3), 6.11 s (1H, CH), 7.38–7.90 m (4H, C_6H_4), 13.27 br.s (1H, OH)
VIIa	1698 (C=O), 3260, 3467 (NH_2)	2.20 s (6H, $2CH_3$), 6.15 s (1H, CH), 7.60–8.05 m (5H, C_6H_5), 7.76 s, 7.90 s (2H, NH_2)
VIIb	1693 (C=O), 3260, 3464 (NH_2)	2.20 s (6H, $2CH_3$), 2.40 s (3H, CH_3), 6.14 s (1H, CH), 7.39–7.94 m (4H, C_6H_4), 7.73 s, 7.87 s (2H, NH_2)
VIIc	1660 (C=O), 3314 (NH)	2.18 s (6H, $2CH_3$), 4.43 d (2H, CH_2), 6.14 s (1H, CH), 7.24–8.06 m (10H, $2C_6H_5$), 9.14 br.s (1H, NH)
VIId	1678 (C=O), 3403 (NH)	2.18 s (6H, $2CH_3$), 2.39 s (3H, CH_3), 4.43 br.s (2H, CH_2), 6.13 s (1H, CH), 7.25–7.96 m (9H, C_6H_4, C_6H_5), 9.10 br.s (1H, NH)
VIIe	1679 (C=O)	2.24 m (9H, $3CH_3$), 6.19 s (1H, CH), 7.15–8.12 m (9H, C_6H_4, C_6H_5), 10.36 s (1H, NH)
VIIf	1672 (C=O)	2.23–2.40 m (12H, $4CH_3$), 6.17 s (1H, CH), 7.16–7.99 m (8H, $2C_6H_4$), 10.29 s (1H, NH)
VIIIa	1660 (C=O), 3168, 3398 (NHass., OHass.)	2.28 d (6H, $2CH_3$), 5.86–5.89 m (1H, CH), 6.25 s (1H, CH), 7.59–8.07 m (5H, C_6H_5, 1H, OH), 9.03 d (1H, NH)
VIIIb	1664 (C=O), 3168, 3300 (NHass., OHass.)	2.22–2.40 m (9H, $3CH_3$), 5.87 m (1H, CH), 6.23 s (1H, CH), 7.39–7.98 m (5H, C_6H_4, OH), 8.90 br.s (1H, NH)
Xa	1673 (C=O), 2229 (CN)	2.25 s (6H, $2CH_3$), 6.22 s (1H, CH), 7.63–8.08 m (5H, C_6H_5), 10.89 s (1H, NH)
XIIa	2222 (CN)	2.21 s (6H, $2CH_3$), 3.40–3.72 m [8H, $O(CH_2)_4N$], 6.21 s (1H, CH), 7.62–8.06 m (5H, C_6H_5)
XIIb	2225 (CN)	1.59 br.s, 3.38 br.s [10H, $(CH_2)_5N$], 2.23 d (6H, $2CH_3$), 2.40 s (3H, CH_3), 6.22 s (1H, CH), 7.41–7.92 m (4H, C_6H_4)
XIIIa	1640–1800, 3000–3600 (no bands)	2.21 s (6H, $2CH_3$), 3.44–3.66 m [14H, $O(CH_2)_4N$, $2OCH_3$], 6.20 s (1H, CH), 7.60–8.09 m (5H, C_6H_5)
XIIIb	1640–1800, 3000–3600 (no bands)	1.57–3.66 m [16H, $(CH_2)_5N$, $2OCH_3$], 2.23 br.s (6H, $2CH_3$), 6.14 s (1H, CH), 7.60–8.08 m (5H, C_6H_5)

[a] Band with shoulder.

Methyl 2-aryl-5-hydrazino-1,3-oxazole-4-carboxylates (IIa, IIb) were obtained as described in [9].

Methyl 2-aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carboxylates acids (IIIa, IIIb). A mixture of 0.01 mol of compound **IIa, IIb**, 0.03 mol of acetylacetone, and 1 ml of acetic acid in 20 ml of dry methanol was refluxed for 6 h. After cooling the precipitate was filtered off and compounds **IIIa, IIIb** were purified by crystallization. Additional amount of the products was isolated from the filtrate.

Methyl 5-amino-2-aryl-1,3-oxazole-4-carboxylates (IVa–IVf). A mixture of 0.002 mol of compound **IIIa, IIIb** and 0.01 mol of the corresponding amine in 10 ml of dry dioxane was refluxed for 18 h, dioxane and excess of amine were removed in a vacuum, the residue was treated with water, compounds **IVa–IVf** were filtered off and purified by crystallization.

2-Aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carboxylic acids (Va, Vb). A mixture of 0.01 mol of compound **IIIa, IIIb** and 0.011 mol of sodium hydroxide in 20 ml of aqueous methanol was refluxed for 4 h, cooled, acidified by acetic acid to pH ~4–5, methanol was removed in a vacuum, the residue was treated with water, compounds **Va, Vb** were filtered off and purified by crystallization.

2-Aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carbonyl chlorides (VIa, VIb). A mixture of 0.01 mol of compound **Va, Vb** with 10 ml of thionyl chloride was kept at room temperature for 24 h, thionyl chloride removed in a vacuum, the residue was treated with dry benzene, and after removal of solvent in a vacuum compounds **VIa, VIb** were used for further transformations without additional purification.

2-Aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carboxylic acids amides (VIIa–VIIf). *a*. To 50 ml of 25% aqueous ammonia the solution of 0.005 mol of compound **VIa, VIb** in 20 ml of dry dioxane was added dropwise at cooling with ice water under stirring, the mixture was allowed to stay overnight at room temperature, the precipitate formed was filtered off, and compounds **VIIa, VIIb** were purified by crystallization.

b. To the solution of 0.005 mol of the corresponding amine in 10 ml of dry dioxane 0.0075 mol of pyridine and 0.005 mol of compound **VIa, VIb** was added. The solution was heated to boiling and allowed to stay overnight at room temperature, 80 ml of water was added, the precipitate was filtered off, and compounds **VIIc–VIIf** were purified by crystallization.

c. A mixture of 0.005 mol of one of compounds **Va, Vb** and 0.005 mol of 1,1'-carbonyldiimidazole in 20 ml of dry tetrahydrofuran was stirred at 30–40°C for 1 h, to the warm solution 0.005 mol of the corresponding amine was added, the reaction mixture was cooled to 20–25°C and stirred for 12 h at this temperature. The solvent was removed in a vacuum, the residue was treated with water, the precipitate was filtered off, and compounds **VIIc, VIId** purified by crystallization from 2-propanol. The mixed probe of the samples of compounds **VIIc** and **VIId** prepared by methods *b* and *c* did not give depression of the melting point. IR and ^{1}H NMR spectra of the samples were identical.

2-Aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carboxylic acids *N*-(1-hydroxy-2,2,2-trichloroethyl)amides (VIIIa, VIIIb). A mixture of 0.007 mol of one of compounds **VIIa, VIIb**, 10 ml of chloral, and 0.3 ml of concn. sulfuric acid was refluxed for 8 h, cooled to room temperature, 80 ml of water was added, the precipitate formed was filtered off, and compounds **VIIIa, VIIIb** were purified by crystallization.

2-Aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carboxylic acids *N*-(1,2,2,2-tetrachloroethyl)-amides (IXa, IXb). To a suspension of 0.005 mol of compound **VIIIa, VIIIb** in 20 ml of dry benzene 0.01 mol of thionyl chloride was added, the mixture was refluxed for 8 h, cooled to room temperature 20–25°C, treated with 20 ml of dry hexane, the precipitate formed was filtered off, dried, and compounds **IXa, IXb** were used for further transformations without additional purification.

2-Aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazole-4-carboxylic acids *N*-(2,2-dichloro-1-cyanovinyl)amides (Xa, Xb). To a solution of 0.0066 mol of potassium cyanide in 10 ml of water a solution of 0.003 mol of compound **IXa, IXb** in 20 ml of dry dioxane was added dropwise during 10 min at cooling with ice water and under vigorous stirring. The mixture was stirred for 8 h, 70 ml of water was added, the precipitate formed was filtered off, and compounds **Xa, Xb** were purified by crystallization.

***O,O*-Dimethyl-(2,2,2-trichloro-1-{[5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-phenyl-oxazole-4-carbonyl]amino}-ethyl)phosphonate (XI).** A mixture of 0.002 mol of compound **Xa** and 0.0022 mol of trimethyl phosphite in 5 ml of dry benzene was refluxed for 4 h. After

cooling, the mixture was treated with dry hexane, the precipitate formed was filtered off, dried, and compound **XI** was used for further transformations without additional purification.

2-[2-Aryl-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-oxazol-4-yl]-5-morpholino(piperidino)-4-cyano-1,3-oxazoles (XIIa, XIIb). A mixture of 0.001 mol of compound **Xa, Xb** and 0.0035 mol of morpholine or piperidine in 15 ml of dry tetrahydrofuran was stirred at room temperature for 24 h. The precipitate formed was filtered off, treated with water, and compounds **XIIa, XIIb** were purified by crystallization. Additional amount of these compounds was isolated from the filtrate.

4-Dimethoxyphosphoryl-2-[5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-phenyl-1,3-oxazol-4-yl]-5-morpholino(piperidino)-1,3-oxazoles (XIIIa, XIIIb). A mixture of 0.001 mol of compound **XI** and 0.004 mol of morpholine or piperidine in 8 ml of dry tetrahydrofuran was stirred at room temperature for 5 days, the precipitate formed was filtered off, the filtrate was evaporated in a vacuum, the residue was treated with water, the precipitate formed was filtered off, and compounds **XIIIa, XIIIb** were purified by crystallization.

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